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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,728	10/27/2006	Hikaru Matsuda	BJS-159-115	7722

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	
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04/15/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,728	MATSUDA ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18-21 and 23-28* is/are pending in the application.

4a) Of the above claim(s) *6,7 and 24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-16,18-21,23,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's reply filed on 01/14/2010 is acknowledged. Claims 1,2,11-12 and 23 are amended. Claims 17 and 22 are cancelled. Claims 6-7 and 24-26 are withdrawn. Claims 27-28 are newly added.

Claims 1-16,18-21,23-28 are pending. Claims 1-5,8-16,18-21,23, 27 and 28 are under consideration in the instant office action.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method of treatment wherein the disorder is a cardiac myopathy resulting from myocardial infarction and wherein the cells used are skeletal myoblasts, does not reasonably provide enablement for any cardiac disorder other than that resulting from cardiac infarction or for use of any cell type other than skeletal myoblasts. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claims are drawn to a method of treating any of a number of cardiac disorders using a three-dimensional structure comprising any type of adult stem cell. The specification teaches treatment of cardiac damage resulting from ischemia using the claimed structure made using skeletal myoblasts. The specification does not teach treating any type of heart failure other than the effects of ischemia and does not teach use of any cells other than skeletal myoblasts.

The claims encompass use of any adult-derived stem cell. However, not all adult stem cells are capable of differentiating into cardiac muscle or in expressing muscle-specific factors that are essential in carrying out the claimed invention. Mathur and Martin reviewed the state of the art of stem cell therapy to treat cardiac myopathy resulting from ischemia (The Lancet, 2004, 264:183-192). At page 185 (col. 2) the different types of stem cells are discussed with regard to varying potencies of different stem cell types. Very few cells are considered totipotent, some are pluripotent while others are only multipotent or unipotent and are not capable of giving rise to any cell types. The claims broadly encompass any type of stem cell, including those that are known in the art to not give rise to cardiac cell types. The art, however, only supports treatment of the heart with bone-marrow and blood progenitor cells and skeletal myoblasts (see pages 187-188).

The claims also encompass treatment of heart failure, which is broad and encompasses any type of heart disorder that causes the heart to fail. The claims also encompass myocarditis, which is inflammation of the heart. The specification and the art of record fail to teach treatment of the disorders encompassed by the claims. The only disorder the specification and the art of record address with the claimed methodology is myocardial infarction. Myocarditis is often caused by infection and is not marked by loss of cells treatable using sem cell therapy to lead to regeneration of lost tissue. It would require undue experimentation to determine how to treat, and which stem cell to us in treating, any heart disorder other than that relating to myocardial infarction.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5,8-16,18 and 23 remain rejected and newly added claim 27 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/07568 (published 02/01/2001) as evidenced by Carnac, G et al (1998, **Mol. Biol. Cell.**, 9:1891-1902.) The rejection is maintained for reasons of record set forth at pages 2-3 of the office action dated 07/14/2009.

'568 taught a method of preparing transplantable skeletal myoblast cells and fibroblast cells cultured on a surface coated with Poly-L-lysine and laminin (page 2, lines 18-24). Myoblasts and fibroblasts are cells that derive from more potent stem cells as required by claim 8. Myoblast cells were derived from nonmyocardial tissue (skeletal muscle biopsy) of an adult human (page 38) and applied to dogs, meeting the limitations of claim 10. Syngeneic transplant was used as well meeting the limitations of claim 9 (page 41, 43). Skeletal myoblasts inherently express markers including myogenin, MyoD and Myf5 (see Carnac et al, 2002). CD56 and the myosin chain genes are also inherently expressed in myoblasts (claim 13). Because the cells are skeletal myoblasts, the marker would be expressed at levels of at least 50% and 100% of that of skeletal myoblasts as required by claims 12,14 and 15.

Applicant argues that the technique disclosed by '568 is "cell implantation", which is referred to at paragraph [0007] of the instant specification and is discussed with regard to drawbacks of the technique, the drawbacks being those that Applicant asserts are not present with the claimed invention. In response, '568 meets the limitations of the claims. Whether Applicant's consider the art to be "cell transplantation" is irrelevant the teachings of '568 meet the limitations recited in the claims. '569 teaches

making a sheet of myoblast cells that are transplantable to the heart. The layer of cells has biological connections between the cells and the cells are not embedded in a scaffold. Applicant is invited to discern the differences between that which is claimed and the structure taught by the art. The 'technique' discussed by '568 and its drawbacks are not relevant to the instant rejection. '569 teaches use of the myoblast structure in treating heart failure.

Applicant argues that Carnac, as a secondary reference, only teaches that RhoA and serum response factor control selectively the expression of MyoD. The argument is irrelevant as well. Carnac is not used as a secondary reference. Carnac is merely provided as a supporting reference demonstrating skeletal myoblasts inherently express myogenin, MyoD and Myf5 as is required by some dependent claims.

Claims 1-5,8,11-17 and 19-23 remain rejected under 35 U.S.C. 102(b) as being anticipated by US 6,207,451 (March 27, 2001) as evidenced by Carnac, G et al (1998, **Mol. Biol. Cell.**, 9:1891-1902). The rejection is maintained for reasons of record set forth at pages 2-3 of the office action dated 07/14/2009.

'451 teaches a three-dimensional myoblast containing structure consisting of a rolled sheet of myoblasts (col.6-7). Myoblasts and fibroblasts are cells that derive from more potent stem cells as required by claim 8. Myoblast cells were derived from nonmyocardial tissue (limb skeletal muscle) of rat (col. 6). Skeletal myoblasts inherently express markers including myogenin, MyoD and Myf5 (see Carnac et al, 2002). CD56 and the myosin chain genes are also inherently expressed in myoblasts (claim 13). Because the cells are skeletal myoblasts, the marker would be expressed at levels of at least 50% and 100% of that of skeletal myoblasts as required by claims 12,14 and 15.

Applicant discusses the teachings of '451 and states that '451 does not disclose a three-dimensional structure applicable to the heart comprising a cell from a part other than myocardium of an adult, which comprises a cell sheet having a biological connection without a scaffold. In response,

Applicant fails to point out specifically, which claim limitation is not met by '451. '451 teaches a three dimensional sheet of myogenic precursors (not myocardial), having biological connections between the cells and the cells are not part of a scaffold. Thus, it is not clear which claim limitation is not met.

Claim Rejections - 35 USC § 103

Claim 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/07568 (published 02/01/2001) in view of Jin et al (Jour Pharm and Exp Therapeutics, 02/01/2003, 304:654-660).

The limitations of claim 27 are met by '568 as set forth above. '568 does not teach treating the surface of a heart to be treated with HGF.

However, Jin et al teaches the use of HGF in treating hearts suffering from myocardial infarction. Jin et al teach that HGF improves cardiac function following infarction.

It would have been obvious to combine the teachings of '568 in treating the heart with myoblasts with those of Jin et al teaching the positive effects of HGF in treating cardiac ischemia to arrive at the claimed method. One of skill would have been motivated to make such a combination as the two treatments act through different mechanisms to improve cardiac function and repair cardiac damage following cardiac injury. One of skill in the art could reasonably expect a combination of the two treatments to have beneficial effect on patients suffering from myocardial infarction.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632